A Comprehensive *In Silico* Perspective For Discovery of Novel Inhibitory Candidates Targeting Versatile Transcriptional Repressor MBD2

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SUPPLEMENTARY FIGURES

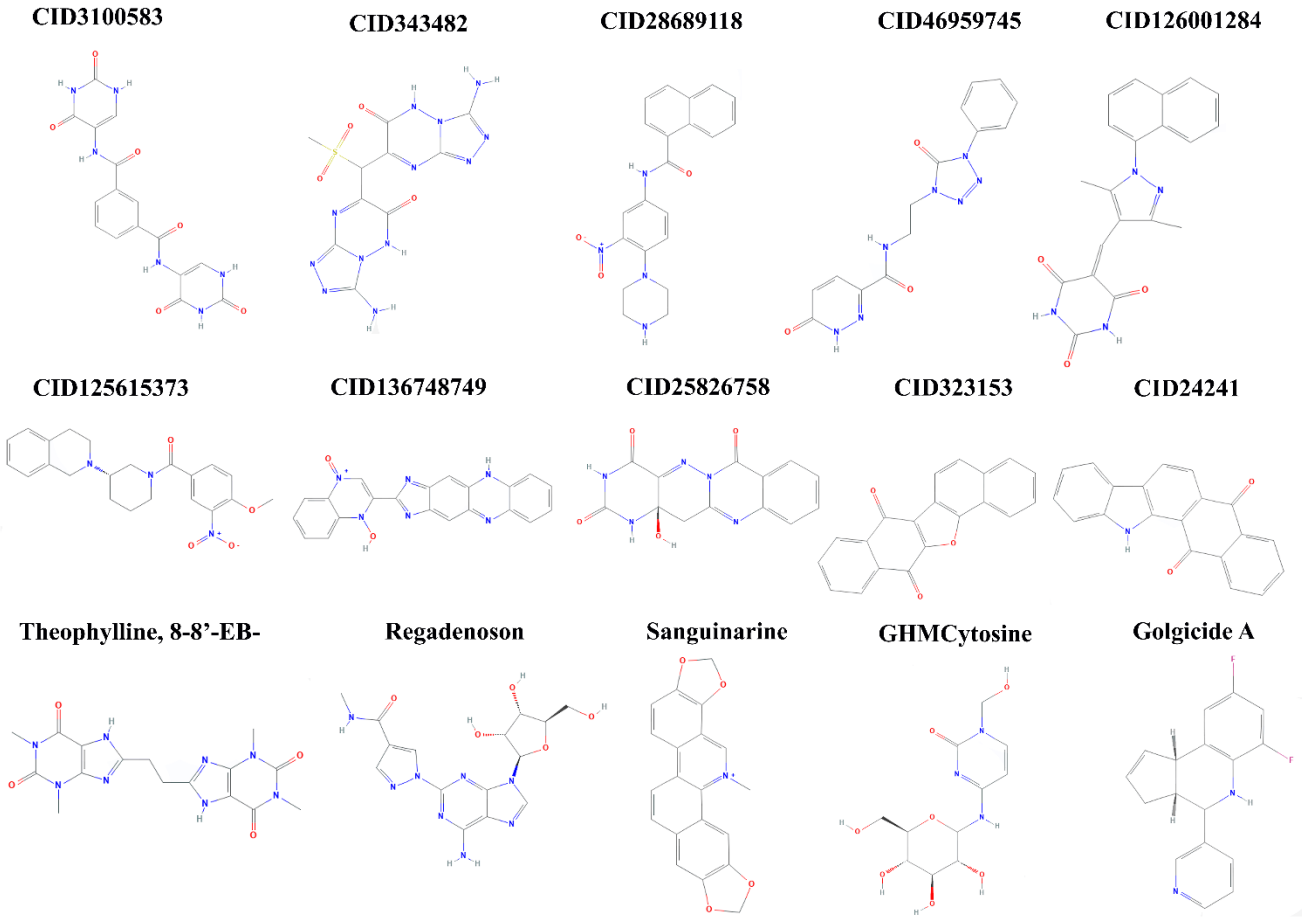

Figure S1. Chemical structures of top compounds acquired in virtual screening.

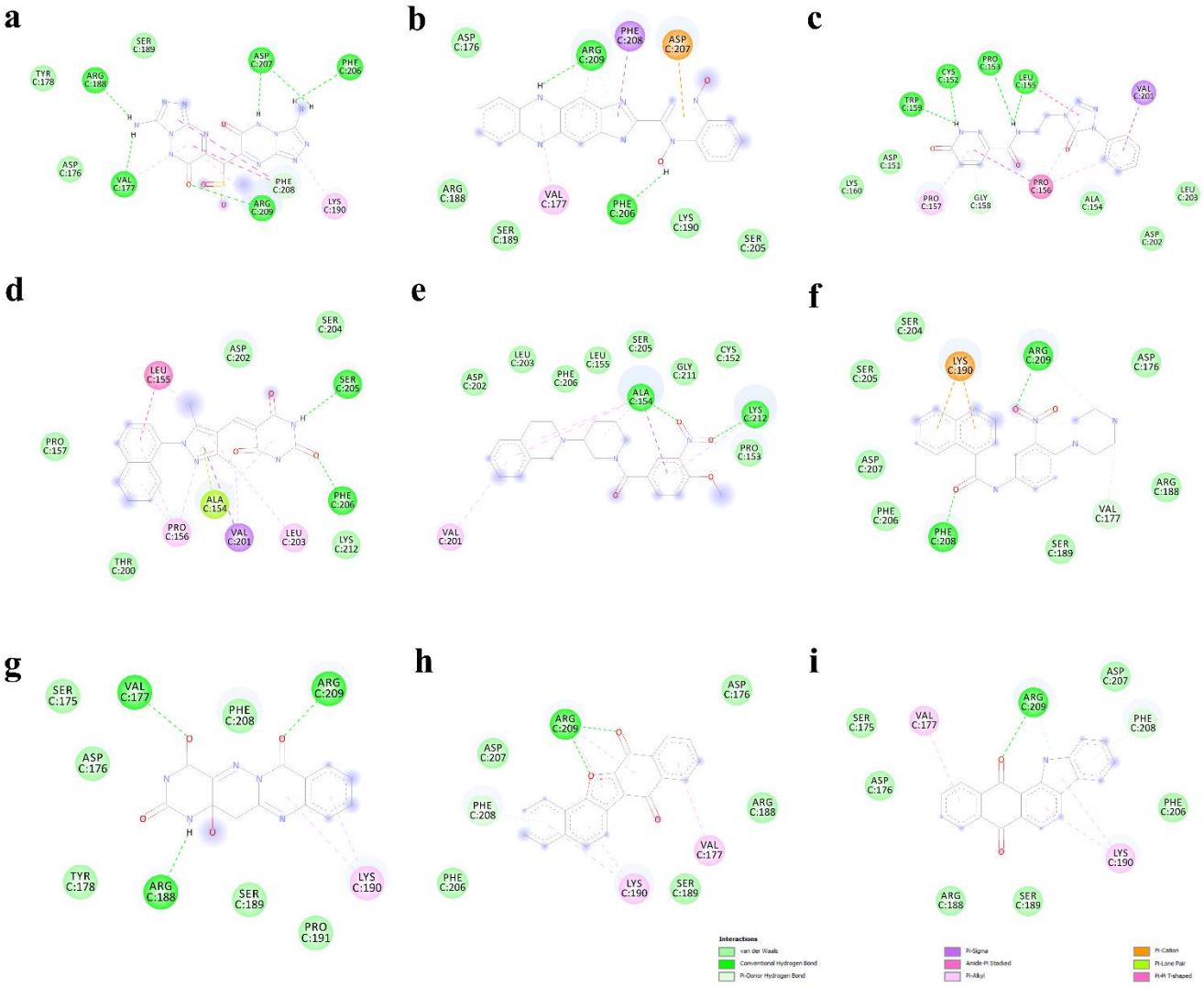

Figure S2. Docking poses in 2D diagram of $MBD2_{MBD}$–ligand complexes with **a)** CID343482 **b)** CID316748749 **c)** CID46959745 **d)** CID126001284 **e)** CID125615373 **f)** CID28689118 **g)** CID25826758 **h)** CID323153 **i)** CID24241.

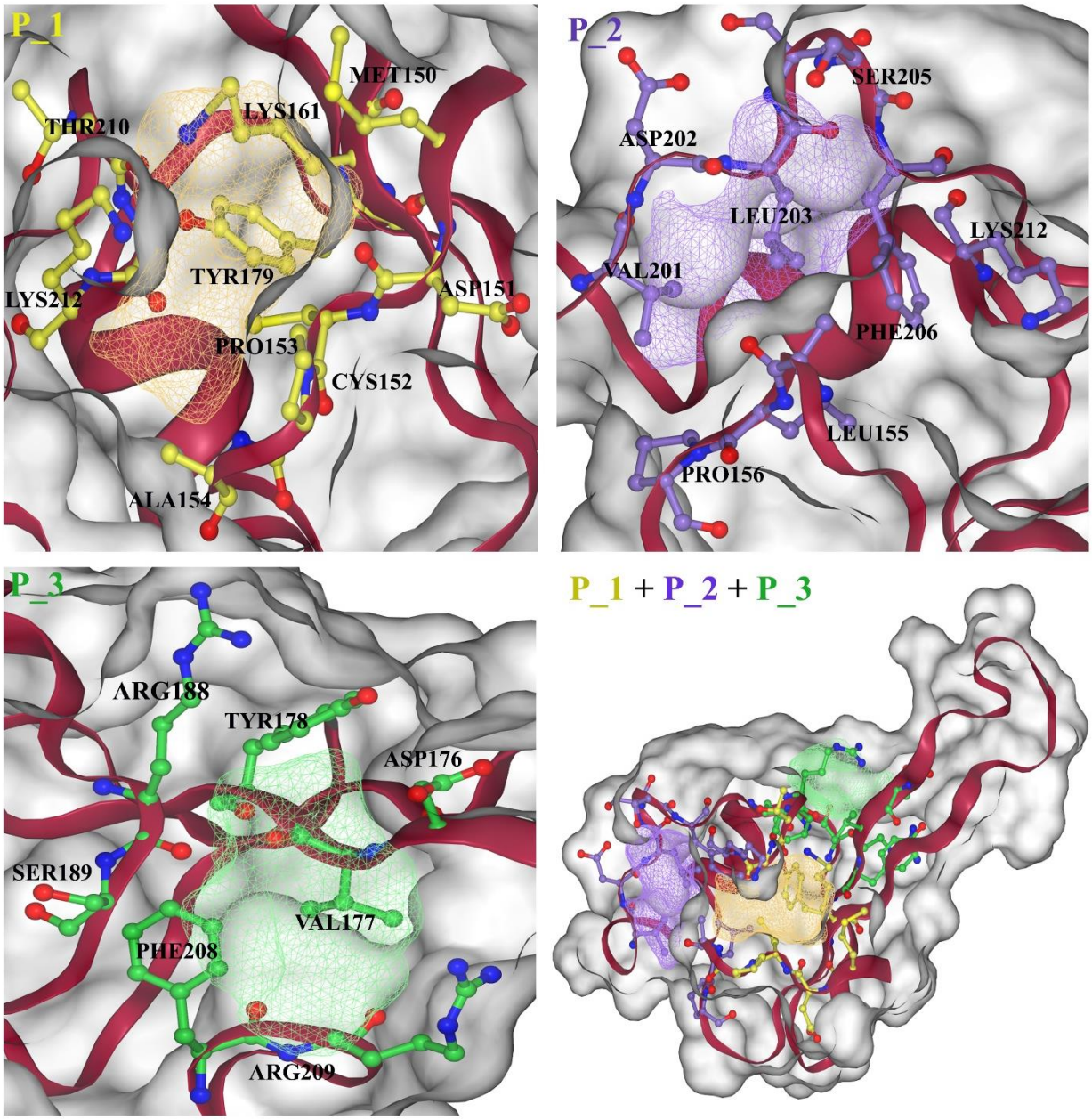

Figure S3. Predicted druggable pockets P_1 (in yellow), P_2 (in violet), P_3 (in green), visualize occupied spaces by singly and overall throughout $MBD2_{MBD}$ receptor. Significant residues in which presumably organize each pockets, have also been indicated in appropriate colors.

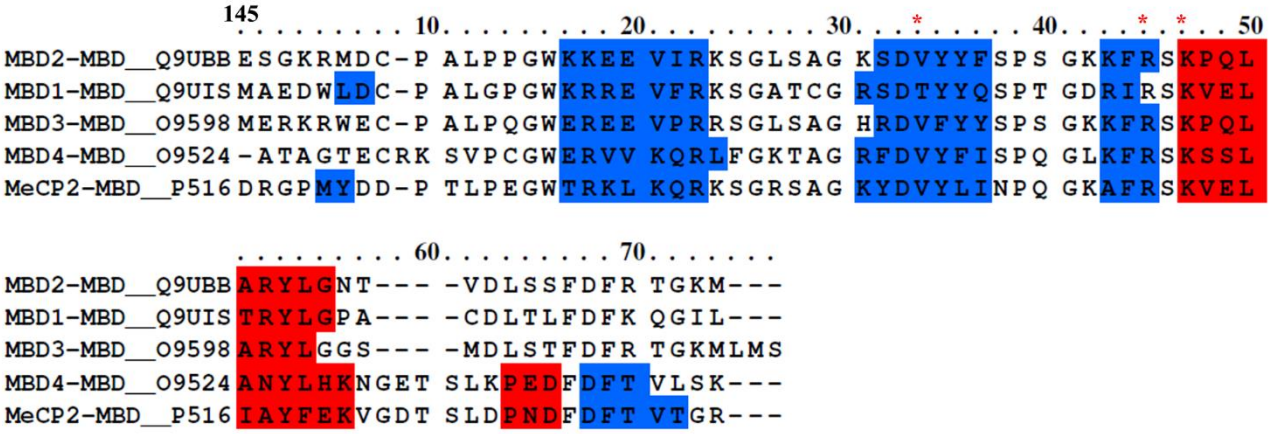

Figure S4. Multiple sequnce analysis of methylated DNA- binding domains (MBD) of MBD family proteins in human. $MBD2_{MBD}$, $MBD1_{MBD}$, $MBD3_{MBD}$, $MBD4_{MBD}$, and $MeCP2_{MBD}$ sequences cover the amino acids between 145–213, 1–69, 1–72, 76–148, and 90–162, respectively. Portions constituted in predicted strands and helices are highlighted with blue and red, respectively. Asterisks remark Val177, Arg188 and Lys190 in $MBD2_{MBD}$, as reference points.

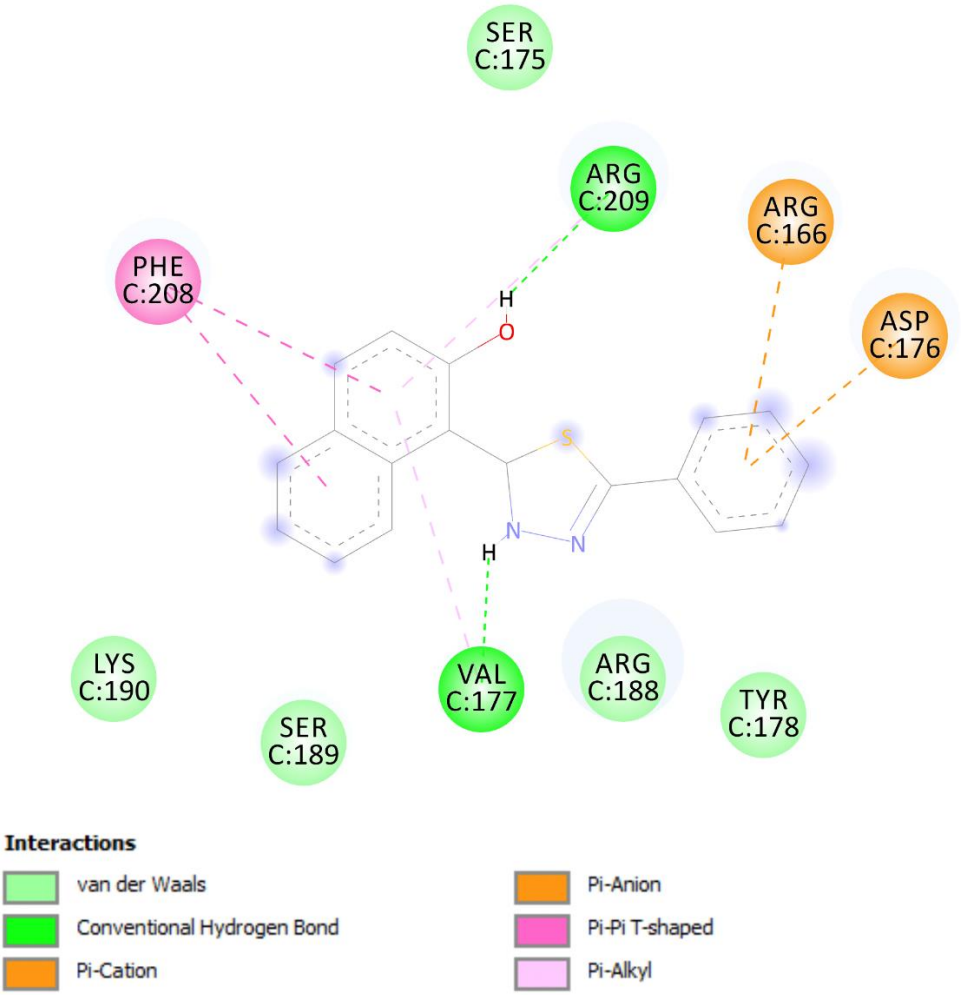

Figure S5. The best docking pose of $MBD2_{MBD}$–CID3136570, a patented compound by Nelson et al.[1], supports our results, comparably signifying the similar binding residues and interactions.

SUPPLEMENTARY TABLES

Table S1. Certain of non-annotated and annotated/identified compounds which have been elucidated by virtual screening (Compounds used in further docking and MD analysis were indicated in bold/italic with asterisks).

A. Non-annotated small molecules

Pubchem ID	IUPAC Name	Molecular Formula	Molecular Weight (Da)	logP	Binding Affinity (kcal/mol)	Net Charge	tPSA (Å^2)
CID24241*	12H-naphtho[3,2-a]carbazole-5,13-dione	C20H11NO2	297.3	4.09	-7.9	0	49
CID323153*	12-oxapentacyclo[11.8.0.02,11.04,9.014,19]henicosa-1(13),2(11),4,6,8,14,16,18,20-nonaene-3,10-dione	C20H10O3	298.3	4.36	-7.9	0	47
CID126001284*	5-[(3,5-dimethyl-1-naphthalen-1-ylpyrazol-4-yl)methylidene]-1,3-diazinane-2,4,6-trione	C20H16N4O3	360.3	2.39	-7.8	-1	95
CID3100583*	1-N,3-N-bis(2,4-dioxo-1H-pyrimidin-5-yl)benzene-1,3-dicarboxamide	C16H12N6O6	384.3	-1.10	-7.7	0	189
CID136748749*	4-hydroxy-3-(10H-imidazo[4,5-b]phenazin-2-yl)quinoxalin-1-ium 1-oxide	C21H13N6O2+	381.4	1.70	-7.7	+1	93
CID343482*	3-amino-7-[(3-amino-6-oxo-5H-[1,2,4]triazolo[4,3-b][1,2,4]triazin-7-yl)-methylsulfonylmethyl]-5H-[1,2,4]triazolo[4,3-b][1,2,4]triazin-6-one	C10H10N12O4S	394.3	-2.93	-7.6	0	238
CID28689118*	N-(3-nitro-4-piperazin-1-ylphenyl)naphthalene-1-carboxamide	C21H20N4O3	376.4	3.41	-7.3	+1	92
CID46959745*	6-oxo-N-[2-(5-oxo-4-phenyltetrazol-1-yl)ethyl]-1H-pyridazine-3-carboxamide	C14H13N7O3	327.3	-1.11	-7.3	0	127
CID125615373*	[(3S)-3-(3,4-dihydro-1H-isoquinolin-2-yl)piperidin-1-yl]-(4-methoxy-3-nitrophenyl)methanone	C22H25N3O4	395.4	3.26	-7.2	+1	77
CID25826758*	(8R)-8-hydroxy-1,2,5,7,11-pentazatetracyclo[8.8.0.03,8.012,17]octadeca-2,10,12,14,16-pentaene-4,6,18-trione	C13H9N5O4	299.2	-1.31	-7.2	0	125

CID136690160*	2-[(5R)-5-thiophen-2-yl-4,5-dihydro-1H-pyrazol-3-yl]naphthalen-1-ol	C17H14N2OS	294.3	4.04	-7.2	0	44
CID136707272	6-[(2-hydroxy-3-methoxyphenyl)methyl]-2-pyridin-2-yl-3,5,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-one	C20H20N4O3	364.4	2.10	-7.2	+1	92
CID11904039	(3aR,4R,9bS)-8-nitro-4-phenyl-3a,4,5,9b-tetrahydro-3H-cyclopenta[c]quinoline	C18H16N2O2	292.3	4.42	-7.1	0	55
CID135623722	9-[(2S,3S,4R,5S)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-8-[4-(2-hydroxyethyl)piperazin-1-yl]-1H-purin-6-one	C16H24N6O6	396.4	-3.15	-7.0	0	160
CID124903520	[(2R,3R,3aR,6S,6aS)-6-acetyloxy-2-(2,6-dioxo-3H-purin-7-yl)-5-oxo-3,3a,6,6a-tetrahydro-2H-furo[3,2-b]furan-3-yl] acetate	C15H14N4O9	394.3	-1.48	-7.0	0	164
CID136748749	4-hydroxy-3-(10H-imidazo[4,5-b]phenazin-2-yl)quinoxalin-1-ium 1-oxide	C21H13N6O2+	381.4	1.70	-7.0	+1	93
CID685052	4-[(3aR,4R,9bS)-8-methyl-3a,4,5,9b-tetrahydro-3H-cyclopenta[c]quinolin-4-yl]aniline	C19H20N2	276.4	4.40	-7.0	0	38
CID5989013	(9E)-9-(pyridin-3-ylmethylidene)fluoren-2-amine	C19H14N2	270.3	4.23	-7.0	0	38
CID865238	1,4,8-trimethylquinolino[2,3-b]quinolin-12-amine	C19H17N3	287.4	4.44	-7.0	0	51
CID124940682	(6S)-1-acetyl-N-methyl-4-(6-oxo-1H-pyridazine-3-carbonyl)-1,4-diazepane-6-carboxamide	C14H19N5O4	321.3	-1.56	-7.0	0	115
CID124239146	(7S)-2-methyl-1'-(2-methylpyrazole-3-carbonyl)spiro[6,9-dihydro-[1,4]oxazino[3,4-c][1,2,4]triazine-7,3'-pyrrolidine]-3,4-dione	C15H18N6O4	346.3	-1.51	-7.0	0	104
CID135774236	2-amino-9-[(2S,3S,4S,5S)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-8-(4-methylpiperazin-1-yl)-1H-purin-6-one	C15H23N7O5	381.4	-2.93	-6.9	0	165
CID98395061	methyl 2-[(1R,3R)-3-[(7aS)-3-amino-5-oxo-1,7a-dihydroimidazo[2,1-c][1,2,4]triazol-6-yl]-2-oxocycloheptyl]-2-oxoacetate	C14H17N5O5	335.3	-1.45	-6.9	0	143
CID136732748	2-amino-9-[(2S,3S,4S,5S)-5-(azidomethyl)-3,4-dihydroxyoxolan-2-yl]-1H-purin-6-one	C10H12N8O4	308.2	-0.95	-6.9	0	149
CID92529390	(2R,6R,8S,12S)-4,10-bis(hydroxymethyl)-4,10-diazatetracyclo[5.5.2.02,6.08,12]tetradec-13-ene-3,5,9,11-tetrone	C14H14N2O6	306.2	-2.10	-6.9	0	115

CID129505580	5-[5-[(1S)-1-amino-3-methylsulfonylpropyl]-1,2,4-oxadiazol-3-yl]-1-methylpyrimidine-2,4-dione	C11H15N5O5S	329.3	-1.03	-6.8	0	153
CID92043634	4-methyl-7-[(2R,3R,5S,6R)-2,3,4,5,6-pentahydroxycyclohexyl]oxychromen-2-one				-6.8		
CID1853030	(4R,4aR,8aS)-2',2'-dimethylspiro[2,3,4a,6,7,8a-hexahydropyridazino[4,5-d]pyridazine-4,4'-oxane]-1,5,8-trione				-6.8		
CID3373552	1,3,4,6,8,9,11,13,14-nonazatetracyclo[10.3.0.02,6.07,11]pentadeca-2,4,7,9,12,14-hexaene-5,10,15-triamine				-6.8		
CID110133179	N-[(3R,4R)-1-(2H-benzotriazole-5-carbonyl)-4-hydroxypyrrolidin-3-yl]methanesulfonamide				-6.7		
CID9569411	(NZ)-N-[5-(hydroxyamino)-1-[2-[(5Z)-3-(hydroxyamino)-5-hydroxyimino-2,6-dihydropyrazin-1-yl]ethyl]-2,6-dihydropyrazin-3-ylidene]hydroxylamine				-6.7		
CID46952388	[3-(hydroxymethyl)-6,8-dihydro-5H-[1,2,4]triazolo[4,3-a]pyrazin-7-yl]-[5-(tetrazol-1-yl)-1H-pyrazol-4-yl]methanone				-6.7		
CID92258087	(2S,3R,4S,5S)-2-(3,4,5,6,8,10-hexazatricyclo[7.3.0.02,6]dodeca-1(9),2,4,7,11-pentaen-10-yl)-5-(hydroxymethyl)oxolane-3,4-diol				-6.7		
CID135708332	9-[(2R,3S,4S,5S)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-8-pyrrolidin-1-yl-1H-purin-6-one				-6.7		
CID1510046	N-[(2R,3R,5S)-2-(hydroxymethyl)-5-(5-methyl-2,4-dioxopyrimidin-1-yl)oxolan-3-yl]methanesulfonamide				-6.6		
CID1519719	(3R)-3-[4-[(3S)-2,5-dioxopyrrolidin-3-yl]-1,4-diazepan-1-yl]pyrrolidine-2,5-dione				-6.6		
CID5354910	1,9-dihydropyrimido[5,4-g]pteridine-2,4,6,8-tetrone				-6.6		
CID1918317	(2S,6S,8R,12R)-4,10-bis(2-hydroxyethyl)-4,10-diazatetracyclo[5.5.2.02,6.08,12]tetradec-13-ene-3,5,9,11-tetrone				-6.5		

CID51491413	[(2R,3S,4S,5S)-5-(5-amino-3-oxo-1,2,4-triazin-2-yl)-3,4-dihydroxyoxolan-2-yl]methyl benzoate				-6.5		
CID92245913	1-[(2S,3S,4S,5S)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]quinazoline-2,4-dione				-6.5		
40646637	(4R,5R)-9-(pyridine-3-carbonyl)-3,4,5,7-tetrahydropurine-2,6,8-trione				-6.4		
323197	3-(2,3-dihydro-1H-tetrazol-5-yl)-6-(2H-tetrazol-5-yl)-1,2,4,5-tetrazine				-6.4		
92542356	(2R,6R,8S,12R)-4,10-diazatetracyclo[5.5.2.02,6.08,12]tetradec-13-ene-3,5,9,11-tetrone				-6.4		
7065057	(2S,3S,4R,5R,6R)-2-(hydroxymethyl)-6-(3-nitroanilino)oxane-3,4,5-triol				-6.4		
136842752	2-amino-9-[(2R,3S,4R,5S)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-8-(hydroxyamino)-1H-purin-6-one				-6.4		
40580751	2-[[(5R)-5-acetamido-4,6-dioxo-1H-pyrimidin-2-yl]sulfanyl]-N-pyrimidin-2-ylacetamide				-6.4		
11865662	N-[(1R,5R,6R)-3-[(2-amino-2-oxoethyl)carbamoyl]-5,6-dihydroxycyclohex-2-en-1-yl]-4-methylbenzamide				-6.4		
125417681	1-[4-[[(2S,3R,4S)-3-hydroxy-4-[(1-methylimidazol-2-yl)methylamino]oxolan-2-yl]methyl]piperazin-1-yl]ethanone				-6.3		
124227847	(7R)-2-methyl-1'-[(1-methylpyrazol-4-yl)methyl]spiro[6,9-dihydro-[1,4]oxazino[3,4-c][1,2,4]triazine-7,3'-pyrrolidine]-3,4-dione				-6.3		
94037351	(1S,8R,9S)-5,12-dimethyl-3,5,7,10,12,14-hexazapentacyclo[7.5.2.01,8.03,7.010,14]hexadec-15-ene-4,6,11,13-tetrone				-6.3		
98395062	methyl 2-[(1S,3R)-3-[(7aS)-3-amino-5-oxo-1,7a-dihydroimidazo[2,1-c][1,2,4]triazol-6-yl]-2-oxocycloheptyl]-2-oxoacetate				-6.3		
6451092	5-[(E)-2-bromoethenyl]-1-[(2R,4S,5R)-4-hydroxy-5-(hydroxymethyl)oxolan-2-yl]-4-(1,2,4-triazol-1-yl)pyrimidin-2-one				-6.2		

92285991	(2S)-N-[(2R)-1-[(2S)-2-carbamoylpyrrolidin-1-yl]-1-oxopropan-2-yl]-5-oxopyrrolidine-2-carboxamide				-6.2		
40646638	(4S,5S)-9-(pyridine-3-carbonyl)-3,4,5,7-tetrahydropurine-2,6,8-trione				-6.2		
25826758	(8R)-8-hydroxy-1,2,5,7,11-pentazatetracyclo[8.8.0.03,8.012,17]octadeca-2,10,12,14,16-pentaene-4,6,18-trione				-6.2		
674379	1-morpholin-4-yl-2-([1,2,5]oxadiazolo[3,4-d]pyrimidin-7-ylamino)oxyethanone				-6.2		
37029880	N-[(4S,5R)-9-acetyl-6-oxo-4,5-dihydro-1H-purin-2-yl]acetamide				-6.2		
75573031	2-(5-aminotetrazol-1-yl)imino-3a,4,5,6,7,7a-hexahydroindene-1,3-dione				-6.2		
136774427	(6S,7S)-6,7-dihydroxy-6-methyl-5,7-dihydro-1H-imidazo[1,2-a]purin-9-one				-6.2		
9569732	(4Z)-4-(diaminomethylidenehydrazinylidene)-6,7-dihydro-5H-indazole-1-carboximidamide				-6.2		
110133230	N-[(3R,4R)-1-acetyl-4-hydroxypyrrolidin-3-yl]-1H-pyrazole-5-carboxamide				-6.2		
129541005	(7S)-N,8-dimethyl-2-(1H-pyrazole-5-carbonyl)-5-oxa-2,8-diazaspiro[3.5]nonane-7-carboxamide				-6.1		
110132954	N-[(3R,4R)-1-[2-(dimethylamino)pyrimidine-5-carbonyl]-4-hydroxypyrrolidin-3-yl]acetamide				-6.1		
137059939	2-amino-8-piperazin-1-yl-1,7-dihydropurin-6-one				-6.1		
135443007	N-carbamoyl-5-oxo-4H-[1,2,5]oxadiazolo[3,4-b]pyrazine-6-carboxamide				-6.0		
135951563	6-hydroxy-5-(1H-1,2,4-triazol-5-yliminomethyl)-1H-pyrimidine-2,4-dione				-6.0		
4209832	1-(diaminomethylidene)-2-(2H-tetrazol-5-yl)guanidine				-6.0		

B. Annotated and/or Biologically Identified Small Molecules

IUPAC Name	Molecular Formula	Molecular Weight (Da)	logP	Binding Affinity (kcal/mol)	Net Charge	tPSA (Å^2)
1,2-Benzanthraquinone	C18H10O2	258.2	3.61	-7.6	0	34
Sanguinarine*	C20H14NO4+	332.3	3.42	-7.5	1	40
8,8'-Ethylenebistheophyline*	C16H18N8O4	386.3	-1.98	-7.3	0	145
Golgicide A*	C17H14F2N2	284.3	4.18	-7.2	0	24
Regadenoson (Lexiscan)*	C15H18N8O5	390.36	-2.43	-7.1	0	186
Lycorcidinol (Narciclasine)	C14H13NO7	307.2	-1.28	-6.8	0	128
4,4'-Bis(Nitramino)Azofurazan	C4H2N10O6	286.1	0.075	-6.8	0	218
Succinoguanamine	C8H12N10	248.2	-1.82	-6.8	0	181
Pancratistatin	C14H15NO8	325.2	-2.22	-6.7	0	148
Skimmin	C15H16O8	324.2	-1.03	-6.6	0	129
Rhamnosyl p-toluensulfonate	C13H18O7S	318.3	-0.1	-6.6	0	122
7,8-Dihydrobiopterin	C9H13N5O3	239.2	-1.41	-6.6	0	136
Wyosine	C14H17N5O5	335.3	-1.69	-6.5	0	126
8-(Methylamino)guanosine	C11H16N6O5	312.2	-2.64	-6.5	0	167
Thiosangivamycin	C12H15N5O4S	325.3	-1.74	-6.4	0	152
TB6:RiboPyrimidoP	C13H13N5O5	319.2	-1.95	-6.4	0	133
Toyocamycin	C12H13N5O4	291.2	-1.50	-6.4	0	150
2-Nitrophenylgalactoside	C12H15NO8	301.2	-1.22	-6.4	0	142
6-Pyrrolizinouridine	C13H19N3O6	313.3	-1.50	-6.4	0	123
Adenosine 5'-monophosphoramide	C10H16N7O5P	345.2	-1.93	-6.3	0	198
5,6-Trimethyleneuridine	C12H16N2O6	284.2	-2.36	-6.3	0	119
7,8-Dihydro-7-methyl-6-thioguanosine	C11H17N5O4S	315.3	-1.62	-6.3	0	159
Glucovanillin	C14H18O8	314.3	-1.31	-6.2	0	125
Glucosylhydroxymethylcytosine*	C11H17N3O7	303.2	-2.90	-6.2	0	155
Fludarabine Base	C10H12FN5O4	285.2	-1.84	-6.2	0	139
6-Mercapto-7-Methylguanosine	C11H16N5O4S+	313.3	-2.26	-6.1	+1	133
8-Chloroguanosine	C10H12ClN5O5	317.7	-2.03	-6.1	0	152
Tubercidin	C11H14N4O4	266.2	-1.37	-6.1	+1	126
8-Azaguanosine	C9H12N6O5	284.2	-3.29	-6.1	0	168
Glycylphenylalanylglycine	C13H17N3O4	279.3	-1.13	-6.1	0	122

5'-N-Methylcarboxamidoadenosine (MECA)	C11H14N6O4	294.3	-1.10	-6.1	0	148
Hypoxanthosine (Inosine)	C10H12N4O5	268.2	-1.30	-6.1	0	129
Clitidine				-6.1		
5-Hydroxycytidine				-6.1		
Primapterin				-6.1		
Mitindomide				-6.1		
5-Methylaminomethyluridine				-6.0		
2-Methylguanosine				-6.0		
2-Methylformycin				-6.0		
5'-Deoxy-8,5'-cycloadenosine				-6.0		
2-Phenylanthraquinone				-6.0		
Hydroxyperylenequinone				-6.0		
Versiquinazoline I				-6.0		
Xanthosinsaure				-6.0		
Valparicine				-6.0		
Thiosangivamycin				-6.0		
Mitomycinone				-6.0		
Isovaleriansaures Coffein				-6.0		
Ribavirin				-5.9		
6-Methoxy-7-nitro-1,4-dihydroquinoxaline-2,3-dione				-5.9		
Bis(imidazolidin-2-ylidene hydrazone)				-5.9		
Mitoguazone				-5.8		
Luciopterin				-5.7		
Cyanomelamine				-5.7		
6-Dimethyltetrahydropterin				-5.7		
1-Tetracene				-5.7		
3,4-Pyridazinedicarboxamide				-5.7		
1,2,5,8-Naphthalenetetrone				-5.6		
Glyoxal-bis(guanylhydrazone)				-5.6		
Deisopropylhydroxyatrazine				-5.5		
8-Hydroxy-7-Methylguanine				-5.5		
6-Hydroxymethylpterin (Ranachrome 3)				-5.5		

Table S2. Calculated MM-PB(GB)SA binding free energy results (kcal.mol^{-1}) for MBD2$_{MBD}$–ligand complexes

Ligand	ΔE_{ELE}	ΔE_{VDW}	ΔE_{GAS}	ΔE_{PB}	ΔE_{GB}	ΔE_{SOL}	ΔE_{TOT}	TS	ΔG_{Bind}
3100583	-3.87 ±1.92	-34.49 ±3.1	-38.36 ±3.83	12.26 ±2.00	-26.10 ±3.16	9.75 ±1.67	-28.61 ±3.00	16.35 ±1.74	-12.26
343482	-5.03 ±5.76	-24.37 ±4.57	-29.40 ±7.44	11.62 ±5.84	-17.78 ±3.34	14.97 ±6.20	-14.43 ±3.62	15.09 ±2.04	0.66
136748749	-3.22 ±2.64	-31.92 ±2.46	-35.14 ±3.76	12.84 ±2.68	-22.30 ±2.30	8.32 ±2.44	-26.81 ±2.32	12.93 ±1.75	-13.88
46959745	-1.77 ±1.35	-21.00 ±6.29	-22.76 ±6.24	5.79 ±2.52	-16.98 ±4.15	3.93 ±1.42	-18.83 ±5.28	7.67 ±2.16	-11.16
126001284	-6.23 ±1.54	-31.83 ±2.38	-38.07 ±3.04	14.42 ±2.11	-23.64 ±2.45	10.58 ±1.67	-27.49 ±2.14	9.26 ±0.86	-18.23
125615373	7.41 ±8.89	-29.47 ±3.79	-22.06 ±11.05	0.98 ±7.66	-21.08 ±5.43	-0.35 ±7.78	-22.40 ±5.04	10.39 ±1.94	-12.01
25826758	-3.88 ±2.08	-24.50 ±4.11	-28.38 ±4.29	9.18 ±2.51	-19.20 ±2.87	7.99 ±1.70	-20.39 ±3.71	12.14 ±2.57	-8.25
323153	-1.41 ±1.72	-17.29 ±4.15	-18.7 ±4.65	4.89 ±2.64	-13.81 ±2.75	4.22 ±1.81	-14.48 ±3.42	9.10 ±2.21	-10.09
24241	-4.12 ±2.05	-26.97 ±2.69	-31.09 ±3.98	11.57 ±2.38	-19.52 ±2.72	7.69 ±1.76	-23.40 ±2.57	12.65 ±1.62	-10.15
Ebis-Theophyl.	-1.86 ±2.03	-37.55 ±3.15	-39.42 ±3.04	11.21 ±1.58	-28.21 ±2.88	8.87 ±1.57	-30.55 ±2.74	15.52 ±2.64	-15.03
Sanguin.	-1.29 ±1.47	-28.08 ±2.76	-29.37 ±2.77	10.08 ±1.76	-19.29 ±2.35	6.83 ±1.15	-22.54 ±2.39	14.29 ±1.39	-8.25
GolgicideA	-4.57 ±1.99	-26.93 ±2.43	-31.50 ±3.53	12.20 ±2.18	-19.30 ±2.42	7.91 ±1.64	-23.59 ±2.34	12.70 ±1.51	-10.89

ΔE_{ELE}: Electrostatic energy, **ΔE_{VDW}:** Van der Waals contribution, **ΔE_{GAS}:** Total gas phase energy, **ΔE_{PB}/ΔE_{GB}:** Non-polar/polar contributions to solvation, respectively, **ΔE_{TOT}:** $\Delta E_{ELE}+\Delta E_{VDW}+\Delta E_{SOL}$, **TS:** Entropic contribution, and **ΔG_{Bind}:** Total estimated binding free energy.

Table S3. Estimation of adverse effects through ADMET-prediction.

	Medicinal Chemistry			Absorption			Distribution		Metabolism				Excretion		Toxicity						
Compound	QED	Pfizer Rule	PAINS Alert	Caco-2 Permeability	Pgp-inhibitor	HIA	PPB (%)	BBB Penetration	CYP1A2 inhibitor	CYP1A2 substrate	CYP2C19 inhibitor	CYP2C19 substrate	CL	$T_{1/2}$	hERG	H-HT	LI	Sk	Re	Ca	Ey
CID3100583	0.332	Acc	–	-6.209	0.002	0.99	27.6	0.002	0.022	0.989	0.059	0.033	5.84	0.96	0.026	0.1	0.96	0.39	0.011	0.02	0.01
CID343482	0.199	Acc	–	-7.08	0.001	0.72	60.8	0.259	0.0	0.547	0.008	0.025	1.01	0.907	0.004	1.0	0.99	0.05	0.923	0.97	0.05
CID136748749	0.258	Acc	–	-5.304	0.372	0.013	95.9	0.295	0.988	0.41	0.025	0.05	3.13	0.563	0.048	0.32	0.12	0.03	0.646	0.95	0.838
CID46959745	0.615	Acc	–	-5.698	0.002	0.434	28.9	0.61	0.039	0.074	0.049	0.053	3.87	0.86	0.026	0.71	0.99	0.15	0.361	0.19	0.017
CID126001284	0.488	Acc	–	-5.769	0.002	0.034	94.8	0.021	0.85	0.756	0.353	0.063	4.56	0.81	0.025	0.86	0.99	0.81	0.669	0.75	0.031
CID125615373	0.587	Acc	–	-4661	0.788	0.011	84.3	0.917	0.274	0.916	0.593	0.822	4.54	0.53	0.976	0.797	0.64	0.71	0.87	0.74	0.012
CID28689118	0.538	Acc	–	-5.278	0.783	0.038	88.1	0.674	0.839	0.753	0.821	0.259	3.96	0.08	0.947	0.928	0.96	0.95	0.82	0.61	0.063
CID25826758	0.556	Acc	–	-6.08	0.001	0.013	84.1	0.87	0.058	0.943	0.029	0.212	1.38	0.67	0.008	0.164	0.96	0.14	0.74	0.76	0.009
CID323153	0.427	Rej	Thiol	-4.881	0.981	0.011	99.5	0.041	0.964	0.154	0.526	0.075	4.49	0.021	0.006	0.95	0.98	0.70	0.044	0.96	0.909
CID24241	0.468	Rej	Quinone-A	-5.06	0.858	0.006	99.6	0.139	0.973	0.207	0.513	0.066	3.02	0.028	0.079	0.84	0.94	0.74	0.176	0.94	0.977
8,8'-Ebis-Theophylline	0.417	Acc	–	-5.733	0.96	0.054	74.4	0.157	0.102	0.993	0.017	0.054	0.85	0.69	0.03	0.22	0.03	0.01	0.672	0.01	0.083
Regadenoson	0.28	Acc	–	-6.208	0.0	0.199	66.9	0.421	0.08	0.09	0.059	0.055	6.29	0.91	0.05	0.77	0.99	0.03	0.086	0.34	0.007
Sanguinarine	0.365	Rej	–	-5.062	0.008	0.002	81.6	0.472	0.985	0.198	0.888	0.605	16.6	0.13	0.04	0.096	0.90	0.77	0.86	0.97	0.87
GHMCytosine	0.33	Acc	–	-5.897	0.004	0.953	12.1	0.534	0.02	0.09	0.019	0.0045	1.62	0.861	0.024	0.931	0.98	0.04	0.078	0.67	0.02
Golgicide A	0.794	Rej	Anil_alk_ene	-4.42	0.012	0.005	96.6	0.9	0.818	0.786	0.913	0.758	5.56	0.16	0.334	0.45	0.43	0.22	0.907	0.11	0.02

Notes **– QED:** Quantitative estimate of drug-likeness (0.67: excellent (green); ≤ 0.67: poor (red)), **Pfizer Rule:** Accepted (logP < 3; TPSA > 75) / Rejected (logP > 3; TPSA < 75, likely toxic), **PAINS:** Pan-assay interference compounds (toxic/reactive compounds existed), **Caco-2 Permeability:** *In vitro* indicator for intestinal cell permeability (>-5.15 log.cm/s: excellent (green); otherwise: poor (red)), **Pgp-inhibitor:** Probability of being of P-glycoprotein inhibitor, a member of ABC transporters (0-0.3: excellent (green); 0.3-0.7: medium (yellow); 0.7-1.0(++): poor (red)), **HIA:** Human intestinal absorption 0-0.3: excellent (green); 0.3-0.7: medium (yellow); 0.7-1.0(++): poor (red)), **PPB:** Plasma protein binding (≤90%: excellent (green); otherwise: poor (red)), **BBB:** Blood-Brain Barrier, logcm/s (0-0.3: excellent (green); 0.3-0.7: medium (yellow); 0.7-1.0(++): poor (red)), **CL:** Clearance of drug (>15 ml/min/kg: high clearance; 5-15 ml/min/kg: moderate clearance; <5 ml/min/kg: low clearance), **$T_{1/2}$:** probability of having extended half-life of drug (0-0.3: excellent (green); 0.3-0.7: medium (yellow); 0.7-1.0(++): poor (red)), **hERG:** human ether-a-go-go related gene blokage as cardiac function marker 0-0.3: excellent (green); 0.3-0.7: medium (yellow); 0.7-1.0(++): poor (red)), **H-HT:** Human hepatotoxicity (0-0.3: excellent (green); 0.3-0.7: medium (yellow); 0.7-1.0(++): poor (red)), **LI:** Human liver injury (0-0.3: excellent (green); 0.3-0.7: medium (yellow); 0.7-1.0(++): poor (red)), **Sk:** Skin sensitization (0-0.3: excellent (green); 0.3-0.7: medium (yellow); 0.7-1.0(++): poor (red)), **Re:** Respiratory toxicity (0-0.3: excellent (green); 0.3-0.7: medium (yellow); 0.7-1.0(++): poor (red)), **Ca:** Carcinogencity (0-0.3: excellent (green); 0.3-0.7: medium (yellow); 0.7-1.0(++): poor (red)); **Ey:** Eye irritation (0-0.3: excellent (green); 0.3-0.7: medium (yellow); 0.7-1.0(++): poor (red)).

Color Legend Scoring **– 0-0.3:** excellent (green); **0.3-0.7:** medium (yellow); **0.7-1.0(++):** poor (red)

References

1. Nelson, W. G., Yegnasubramanian, S., Lin, X., Speed, T. J. & Reichert, Z. Agents for Reversing Epigenetic Silencing of Genes. (2010).